AD-A157 663 A COMPARISON OF RECOMPRESSION THERAPY IN THE TREATMENT OF SPINAL CORD DECOMPRESSION SICKNESS(U) NAVAL MEDICAL RESEARCH INST BETHESDA MD J J SYKES ET AL. JUL 84 1/1

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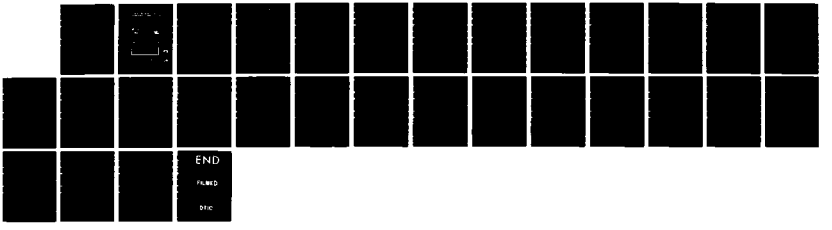

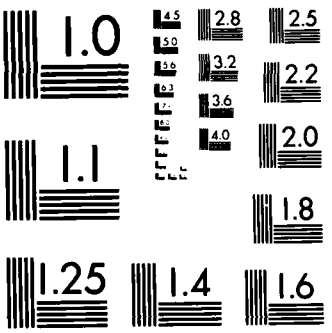

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84-37

A COMPARISON OF RECOMPRESSION THERAPY IN THE TREATMENT OF SPINAL CORD DECOMPRESSION SICKNESS

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Acknowledgements

This study was supported by the Naval Medical Research and Development Command, Work Unit No. M0099PN.01C.0001. The opinions and assertions contained herein are the private ones of the author and are not to be construed as official or reflecting the Navy Department or the naval service at large.

The experiments reported herein were conducted according to the principles set forth in the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council, DHEW, Pub No. (NIH) 78-23.

The author wishes to thank Messrs. Miles, Sloan, Liggett, and Parker, and Mrs. Jones for technical assistance, together with the support of the personnel of the Instrumentation Branch, NMRI, the editorial assistance of Mrs. Maureen Darmody, Mrs. Ellen Hughes, and Ms. Janet Gaines, and Dr. P. Weathersby for advice on data analysis.

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE	READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER: NMRI 84-37	2. GOVT ACCESSION NO.: AD-A157665
	3. RECIPIENT'S CATALOG NUMBER:
4. TITLE (and Subtitle): A COMPARISON OF RECOMPRESSION THERAPY IN THE TREATMENT OF SPINAL CORD DECOMPRESSION SICKNESS	5. TYPE OF REPORT & PERIOD COVERED: MEDICAL RESEARCH PROGRESS REPORT, Final
	6. PERFORMING ORG. REPORT NUMBER:
7. AUTHOR(s): J.J.W. Sykes, J.M. Hallenbeck, and D.R. Leitch	8. CONTRACT OR GRANT NUMBER(s):
9. PERFORMING ORGANIZATION NAME AND ADDRESS: Naval Medical Research Institute, Bethesda, Maryland 20814	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: M0099.01C.0001 Report No.22
11. CONTROLLING OFFICE NAME AND ADDRESS: Naval Medical Research and Development Command, Bethesda, Maryland 20814	12. REPORT DATE: July 1984
	13. NUMBER OF PAGES: 24
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office): Naval Medical Command, Department of the Navy, Washington, D.C. 20372	15. SECURITY CLASS. (of this report): UNCLASSIFIED
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE:

16. DISTRIBUTION STATEMENT (of this Report)

APPROVED FOR PUBLIC RELEASE AND SALE. DISTRIBUTION UNLIMITED.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

evoked potentials; spinal cord; decompression sickness; treatment; oxygen

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

In an animal model spinal evoked responses to peripheral nerve stimulation were used as a measure of spinal cord function before, during, and after a dive profile found to reliably produce spinal cord decompression sickness (DCS). It was determined that progressive loss of amplitude, the major change, indicated the occurrence of spinal cord DCS. After a period of time, to allow the lesion to consolidate and therefore simulate delayed treatment, the animals were recompressed and treated. Treatment Group A

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S/N 0102-LF-014-6601

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(n = 10) consisted of the standard treatment of 100% oxygen at 60 fsw (2.8 ATA) and treatment Group B (n = 8) consisted of 66% oxygen at 66 fsw (2.0 ATA). Serial measurements of spinal evoked responses documented the return of electrophysiological function during the treatment period. Each response was characterized as the sum of the amplitude expressed as a percent of surface control. Results indicated that there was a varied response to treatment regardless of treatment group and that after 25 min of treatment there was not likely to be further significant return of amplitude. Linear regression lines were fitted to the profile beyond 25 min and the intercept and gradient were used to describe the course of treatment. No significant difference was found between the severity of DCS, the surface interval before treatment, or the maximum effect of treatment, although the gradient was found to be different. When regression analysis was extrapolated to 120 min of therapy, however, no difference was found between treatment groups. It was found that the animals responded either well or poorly, regardless of treatment group. The nonresponders showed a more rapid onset of DCS, a more severe insult, and generally were worse off physiologically. The most striking feature was the rise in CSF pressure in this group. Although the findings agree with previous work, the question of a different etiology to explain data from the nonresponders was raised. The failure to differentiate between treatments was discussed together with the relative merits of each one. It was concluded that treatment B had an increased safety margin, although the potential difficulties of introducing it for use in the Fleet probably outweighed the safety advantage.

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INTRODUCTION

Spinal cord injury as the result of decompression sickness (DCS) is a well recognized clinical entity reported as a symptom in 22% (Rivera, 1964) to 50% (Bayne, 1978) of cases. Current therapeutic measures are mainly successful in alleviating symptoms and signs of the disease process when applied correctly, but nevertheless there are a number of patients who do not recover fully and are left with residual motor and sensory deficits. To amateur and professional divers this represents the end of a diving career, a physical handicap, and the subsequent social repercussions of disability and dependence on medical and welfare resources. To the military it results in the loss of highly skilled and expensively trained individuals who cannot be replaced without costly training of other divers.

Clearly, with a disease process that has such social and economic consequences, prevention should be of prime concern. Indeed, considerable research is being directed at improving decompression schedules by the US Navy and others. Because of the probabalistic nature of the disease and the variation in individual susceptibility, however, there is little hope that it can be prevented entirely even under optimum conditions. Much diving takes place under less than ideal conditions, where ignorance, lack of training, or plain stupidity result in diving accidents and diving-related disease, such as DCS. The onus, therefore, lies with improving the therapy of DCS in the first instance while improved methods of prevention are developed.

The current therapy of DCS consists of recompression and the concurrent administration of high concentrations of inspired oxygen together with various pharmacological agents. A diverse selection of therapeutic recompression tables are available for use around the world (Berghage, et al., 1978), and the use of any particular table is governed by local preference and the

circumstances of the patient's presentation and diving history. In addition to the rules laid down in various diving manuals, other guidelines for treatment have been issued (Undersea Medical Society, Inc., 1979). These tables have been developed empirically over the last 50 years, each generation resulting in improved outcomes of therapy. Nevertheless, surveys of their individual efficacies invariably highlight deficiencies that result in further modifications to the therapeutic approach. The development of therapeutic recompression tables has been documented by Davis and Elliott (1982) together with the rationale for their use. Although recompression and oxygen are used in the treatment of decompression sickness, Barnard (1978) has noted that these therapeutic elements have not been tested scientifically as independent variables. Valid comparisons between the various recompression profiles available have not been made either. Such comparison is recognized as difficult to perform because of the relatively few cases, the wide range of severity, and the known efficacy of modern treatment. Until quite recently, animal studies have used relatively crude assessments of success, i.e., death or survival.

Recently, a more sophisticated method of studying the disease process has been developed to study spinal cord DCS in laboratory animals. Evoked responses, generated from peripheral nerve stimulation, have been used as a sensitive indicator of neurophysiological function in the spinal cord both experimentally and clinically for several years. The technique has been developed by Leitch (1984) to study spinal cord decompression sickness in a hyperbaric chamber throughout an exposure to pressure and during the subsequent period of therapy. After establishing a dive profile that resulted in the development of spinal cord DCS, Leitch studied the effects of pressure and oxygen as independent variables in the treatment of DCS. At a fixed

recompression depth of 132 fsw he varied the inspired pO_2 in the range of 1-3 ATA and found an optimum response at 2 ATA. Subsequently, he fixed the inspired pO_2 at 2 ATA and varied the depth of recompression between 66 and 198 fsw (3-7 ATA). At the end of 2 hr of therapy his results indicated that 66 fsw was the optimum depth for recompression. For comparison with the currently accepted treatment regime, Leitch included a group of animals treated with 100% oxygen at 60 fsw (2.8 ATA). Although at 2 hr no difference in outcome was noted between the standard approach and the optimum combination of oxygen and pressure cited previously, he did observe a faster response to treatment with the latter therapy (Leitch, personal communication).

These observations have important implications for the future treatment of DCS. Acute cerebral oxygen toxicity resulting in epileptiform convulsions is a rare complication of exposure to high inspired oxygen tensions during therapeutic recompression. Although no long-term effects have been reported as the result of such convulsions, there is a risk of injury at the time of the attack. The major complication is the necessary interruption to treatment as the result of the convulsion. Exposure to excess oxygen can also result in the development of pulmonary problems, particularly when the exposure is prolonged. With the present tendency to "extend" therapeutic tables in difficult or unresponsive cases, the likelihood of patients developing iatrogenically-induced pulmonary oxygen toxicity is increased. Not only are the symptoms distressing, but the effects on pulmonary function are only slowly reversible. In addition, it is suspected that decompression procedures may be adversely affected in the presence of pulmonary oxygen toxicity (Flynn and Greene, 1981). Should the application of 2 ATA inspired oxygen in conjunction with recompression to 66 fsw prove to be more effective than the current therapy, then its introduction into the treatment regime would result

in a reduced risk of acute cerebral complications and would allow extended long-term exposures before the development of pulmonary complications.

This study was performed to further evaluate Leitch's findings by comparing standard therapy to the optimum combination of oxygen and pressure.

METHOD

Male, mongrel dogs were prepared in a fashion identical to that described by Leitch (1984). Following premedication with atropine (0.05 mg/kg) and xylazine (1.1 mg/kg), the animals were anesthetized with sodium pentobarbitol (13.5 mg/kg), intubated, and respirated mechanically with a modified Ford Mark respirator. End tidal pCO2 was monitored on a Beckman [illegible] analyzer. The respirator was adjusted to maintain the range of [illegible] equivalent CO_2. After the initial dose, anesthesia was maintained by half the initial dose at 20 min, followed by a maintenance dose [illegible] given in divided doses every 20 min. Polyethylene catheters were placed in the left forelimb vein to maintain anesthesia and to administer fluids, and in the left femoral artery to periodically sample blood gases. A catheter was also placed in the right femoral artery to measure systemic blood pressure by a Statham pressure transducer. In addition, a Millar pressure tip catheter was introduced through the right femoral vein and advanced to the right ventricle to measure right ventricular pressure. The rectal temperature was maintained between 37 and 38.5 °C by a hot-water plate incorporated into the base of a head-holding stand where the animal was placed prone, supported by ear bars. The skull was bared of tissue over the sensorimotor cortex area, and a stainless steel screw electrode was placed in a hole drilled in cancellous bone. The indifferent electrode was placed in a hole drilled in the distal nasal bones. Spinal electrodes of insulated stainless steel wire, sharpened at the tip, were placed in adjacent intervertebral spaces in the

region of L1/2, T8, and C7, in the midline, and located so that their tips were embedded in the spinal lamina. Median and peroneal nerves were stimulated through pairs of stainless steel needle electrodes placed percutaneously with the cathode placed proximally. After placement of the electrodes, a needle was introduced into the subdural space through the cisterna magna and connected to a Statham pressure transducer to measure CSF pressure. Pressure measurements, EKG, and EEG were recorded continuously on a Gould Polygraph 8-channel chart recorder.

A Nicolet Stimulus Pulse Generator (NIC 502) was used to drive a Grass S88 stimulator and two computers of average transients (CAT)(Nicolet Models 1072 and 1074). The stimulus, delivered at 2.5/sec through a Grass Photoelectric Stimulus Isolation and Constant Current Unit (PISU 6C) at 120 V, and 10 ma, was directed to the relevant electrodes by a switching box.

After amplification by 10^4 (NIC 200-A) the spinal and cortical electrode signals were further amplified and filtered on a 30-3000 Hz bandpass filter/amplifier (NIC 501-A). The spinal electrode signal was averaged by the 1074 CAT with a 25-30 ms span while the cortical signal was averaged by the 1072 CAT with a 120-ms span. In each case 128 stimuli were stored and displayed on two Tectronics oscilloscopes (5110) and then recorded on Hewlett-Packard X-Y plotters (HP 7045A and B).

After preparation the animal was placed in the pressure chamber (Bethlehem Steel) and various connections were made to the outside. Surface control data were collected and then the animal was submitted to a dive profile designed to cause spinal cord DCS. Compression to 300 fsw was achieved at 75 feet per minute (fpm), followed by 15 min at depth. Decompression was performed to 60 fsw at 60 fpm and then to 2 fsw at 45 fpm. (A small driving pressure was required in the chamber to enable end-tidal

gases to be measured). Evoked potential data were recorded serially throughout the dive and during the subsequent surface interval. The onset of spinal cord DCS was diagnosed when an obvious loss of amplitude occurred in the evoked potential recording. The lesion was allowed to develop and consolidate for 15 min before the treatment regime under evaluation was initiated. At this point, the treatment gas was connected to the ventilator and the animal was compressed to treatment depth. Evoked potential data were then collected at 5 min, 15 min, and every 15 min thereafter up to 2 hr. The experiment was terminated at this point by the injection of a saturated solution of potassium chloride into subject animals. The occurrence of shock or cardiopulmonary embarrassment at any stage was treated with fluids (i.e., lactated Ringers solution or bicarbonate), or short recompression to 60 fsw as appropriate. In the event that DCS did not develop within a 30-min surface interval, the dive profile was repeated with a bottom time of 8 min. Ten animals (Group A) were treated at 60 fsw, breathing cycles of 100% oxygen (2.8 ATA) for 25 min and air for 5 min for a total of 4 cycles (2 hr). Eight animals (Group B) were treated at 66 fsw, breathing 66% oxygen (1.98 ATA) continuously. Another 12 animals either died or were excluded for technical reasons. Death was usually preceded by profound shock, EKG abnormalities, and failure to respond to resuscitation and rapid recompression to 60 fsw.

DATA PROCESSING

I. Evoked potential data.

Each recording of the spinal evoked potential (SEP) was in the form of a multipeaked sine wave with up to 14 easily identifiable peaks, described by latency and amplitude, which were marked, digitized, and stored in a computer (PDP 11/34D) before processing. Because the major change in SEP due to DCS was a loss of amplitude, a simple means of describing that change was to sum

the peak-to-peak amplitude of each of the 14 recognizable peaks in each recording. The mean of the summed amplitude of surface control data was designated 100% and the subsequent summed amplitude at any time point was described as a percent of surface control. Each entry was identified by animal number, phase of experiment, depth, and time into phase.

II. Physiologycal Data.

The use of mongrel dogs introduces a wide variation of "normal" measurements. In order to minimize this effect we used each animal as its own control. For each animal the mean value of a variable was calculated for control and treatment periods and the difference was established, i.e., the effect of treatment on that animal for the variable under consideration. The mean effects on the treatment group as a whole then were calculated and compared statistically (unpaired t-test).

RESULTS

I. Evoked Potentials.

A. Cortical. No data on cortical evoked potentials are presented because in addition to developing spinal cord DCS, the majority of animals suffered cerebral manifestations of DCS revealed by loss of EEG amplitude. After the reduction or loss of EEG signal it was not possible to record cortical evoked responses.

B. Spinal. Loss of amplitude, indicating the onset of DCS, occurred in the lumbar region of 16 animals after the first dive. Two animals required a second dive to induce DCS. The onset of the loss of amplitude began between 3 and 30 min into the surface interval and treatment was initiated 15 min after onset. The mean (± SD) surface intervals before treatment were 23.5 ± 7.7 min (Group A) and 24.5 ± 9.8 min (Group B). After the onset there was a progressive loss of amplitude in the SEP until treatment was started. At the

amplitude, resulting in a favorable response to therapy. Permanent damage, in the form of altered myelin sheaths, will not be influenced by either pressure or hyperbaric oxygen and accounts for the "therapeutic deficit" seen in the response to treatment. The proposed mechanism for the generation of the myelin changes is compatible with the major concepts of bubble interaction, i.e., arterial, venous, or autochthonous models.

CONCLUSIONS

1. This model causes spinal cord DCS that resembles that found in man. It appears to be more severe, however, than that generally observed in patients.

2. This model provides a spectrum of severity of DCS that permits the comparison of various treatment regimes in spinal cord DCS.

3. There is some evidence to suggest that the etiology of DCS may involve more than one mechanism. Although the physiological changes are similar to those reported previously for venous obstruction to blood flow in the spinal cord, there are features that suggest other mechanisms may play a part in deciding the response to treatment.

4. We did not demonstrate a difference between the efficacy of recompression to 60 fsw on 100% oxygen (2.8 ATA) and recompression to 66 fsw on 66% oxygen (2 ATA) in this model of spinal cord DCS. The slight difference in the slope of the response of the two methods did not produce a significantly different outcome after 2 hr of treatment. Exclusion of nonresponding animals from the analysis did not alter the relationship between the two treatment groups under evaluation.

5. There may be a theoretical advantage to treatment at 66 fsw in that there is less risk of both cerebral and pulmonary oxygen toxicity breathing 2 ATA at that depth. Despite the advantage of increased safety, there are potential objections to using a mixed gas for treatment. The principle objection, again

model of spinal cord DCS, one may assume that a similar etiology is involved in this experimental model. The appearance of white-matter hemorrhage and sparing of grey matter (unpublished observations) in spinal cord sections from our animals is similar to findings reported by Hallenbeck et al. (1975), and these findings are compatible with venous infarction (Hensen and Parsons, 1967), which was also considered by Haymaker (1957), although he generally supported the concept of arterial bubble embolism. Extensive damage to white matter has been reported in long-standing cases in man by Lichtenstein and Zetlin (1936), and more recently, Palmer et al. (1981), as well as in animals (Palmer et al., 1978).

Do the responders represent a less severe manifestation of the same syndrome or is a different etiology, more amenable to treatment, responsible? As the physiological changes in this group are not as great as in the nonresponders, the tendency toward hemoconcentration together with a smaller rise in CSF pressure would suggest that a less severe form of venous obstruction within the epidural vertebral venous system was responsible for a lesser degree of DCS. The argument of Hills and James (1982), however, counters the Hallenbeck concept by suggesting that it is difficult to imagine total stagnation in such a multichannel structure as the epidural vertebral venous system. This argument is difficult to refute and suggests that a different etiology may be involved in the nonresponsive group. There is some evidence (Sykes et al., in preparation) to suggest that irreversible changes to the myelin sheath, and hence the ability of the axon to function, may be responsible for the failure to respond to therapy and that the grade of the response may be determined by the relative number of axons affected. Most of the reversible damage is assumed to be ischemic in origin, and therefore, the effects of pressure and oxygen will tend to improve the reduction in SEP

because the mechanisms for the elimination of inert gas may be already compromised as the result of DCS. This theoretical objection to the use of gas mixtures does not appear to dissuade the French from their use of this regime (COMEX Diving Ltd, 1976; Group d'Etudes et Recherches Sousmarine (GERS), 1964). The essential philosophy of the continental approach to treatment involves greater compression using gas mixtures to avoid the toxic repercussions of pure oxygen.

The clear separation of the animals into responsive and nonresponsive groups, regardless of therapy, has important parallels to the experience of divers. As cited earlier, improved therapies for DCS are required, particularly for the fortunately few patients who do not respond fully to conventional therapy. The occurrence of this response in this model adds further conviction for its applicability to the investigation of the therapy of DCS. In addition to the poor response to therapy, the nonresponsive group also appeared to have a more severe form of DCS than the responsive group. This was evident from the degree of injury immediately before treatment. This group also demonstrated a much greater rise in CSF pressure than the responders, along with a lower group mean systolic blood pressure. It is not clear whether these group changes were responsible for the overall poor response to therapy shown by this group, or whether the changes reflect a more severe form of DCS that is less amenable to therapy. The relatively minor changes to the physiological measurements that occurred between treatment Groups A and B suggest that little or no experimental bias was present. The fact that there was no difference evident in the fluid replacement therapy administered to the animals tends to confirm this view.

Because the physiological changes reported here are very similar to those reported by Hallenbeck et al. (1975) in their epidural vertebral venous system

possible safety advantages inherent in the lower pO_2. Given the small difference between the two groups, both in depth of recompression and level of inspired oxygen tension, it is not surprising that there is no apparent difference between the two treatment groups in this series of experiments.

In practical terms there may be an advantage to adopting the treatment for Group B in terms of potential for increased safety in both cerebral and pulmonary oxygen toxicity. Oxygen convulsions are rare, but recognized complications in standard treatments, yet at the same time, they do not contraindicate treatment. The incidence is not known with certainty and little can be done to reduce it, except by reducing the inspired oxygen tension as susceptibility varies between individuals and in the same individual from day to day (Donald, 1947). Therefore, adoption of this treatment option would result in reducing the incidence of an already rare occurrence.

Under certain circumstances the standard oxygen tables are extended by additional periods of oxygen breathing, particularly when response to treatment is slow and when further recompression is likely to be ineffective or undesirable. In this situation the possibility of developing pulmonary oxygen toxicity is much higher and in fact may be used as an end point of therapy. The potential advantage of treatment at a lower inspired oxygen tension lies in increasing the exposure time possible before toxic effects become evident, while at the same time taking advantage of the therapeutic effects of hyperbaric oxygen.

The major objection that could be raised against the introduction of this treatment regime is that the patient is exposed to an inert gas load that must be eliminated safely to avoid recurrence of DCS. It could be argued that exposure to additional inert gas during treatment may prejudice the outcome

the general experience with human DCS. This view may enjoy additional support from the general physiological changes found. Although some animals showed very little change in physiological measurements, the majority did demonstrate often profound changes requiring aggressive fluid support to achieve survival. Often, marked pulmonary effects were also seen, perhaps reflected in the tendency for right ventricular pressures to rise, particularly in the nonresponsive group. In contrast, the human patient rarely demonstrates profound shock, respiratory problems, and hemoconcentration, although when these occur they are considered life threatening and of very serious import when classifying the severity of the disease process. Compared to the usual patient, therefore, this model represents a very severe insult to the animal, and as a result, a severe test of the efficacy of therapy. The wide range of response to therapy, however, may itself be responsible for the inability of this model to differentiate these two treatment regimes.

The rapid response to treatment within the first 15-30 min of treatment, regardless of group, is not an unexpected finding as a return to pressure remains the first choice of treatment. The efficacy of recompression has been recognized since the mid-19th century. The similarity of the depth of recompression between the two groups in this series would suggest that the effects of recompression alone are not likely to be very different. Therefore, whatever possible advantage may be inherent in the respective treatments is likely to be conferred by the level of inspired oxygen tension. Despite Leitch's findings that the optimum combination of oxygen and pressure (Leitch, personal communication) are combined in treatment Group B, the magnitude of the difference between 2 and 2.8 ATA is small compared to the magnitude of either of them relative to normal inspired oxygen tension. The therapeutic difference is, therefore, also likely to be small despite the

TABLE 5

WEIGHT AND SUPPORTIVE TREATMENT BY TREATMENT GROUP AND RESPONSE*

	A	B	Responders	Nonresponders
Weight (kg)	11.35 ± 1.7	10.5 ± 1.05	11.06 ± 1.66	10.84 ± 1.24
Flush (Vol ml)	55 ± 26	62 ± 17	58 ± 24	57 ± 20
Ringers (Vol ml)	121 ± 127	158 ± 151	98 ± 126	198 ± 136
HCO_3 (Vol ml)	26 ± 21	13 ± 18	21 ± 22	19 ± 19

* ($\overline{X}$ ± SD); A, n = 10; B, n = 8; Responders, n = 11; Nonresponders, n = 7

TABLE 4

CONTROL AND TREATMENT VALUES BY RESPONSE*

			Responders	Nonresponders
Aortic Pressure (mm Hg)	(S)	C	142 ± 23	141 ± 15
		Rx	6 ± 15	-8 ± 17
	(D)	C	111 ± 22	110 ± 12
		Rx	4 ± 12	-8 ± 17
Right Ventricular Pressure (mm Hg)	(S)	C	19 ± 7	20 ± 7
		Rx	2 ± 9	-1 ± 4
	(D)	C	2 ± 2	2 ± 1
		Rx	6 ± 5	-<1 ± 2
CSF Pressure (mm Hg)	(S)	C	3 ± 1	7 ± 3
		Rx	5 ± 6	31 ± 15
	(D)	C	3 ± 1	7 ± 3
		Rx	5 ± 5	29 ± 13
Heart Rate		C	128 ± 19	132 ± 33
		Rx	-4 ± 13	-3 ± 12
Rectal Temperature		C	38.09 ± .35	37.92 ± .47
		Rx	-0.24 ± 1.08	0.56 ± 0.45
Hematocrit		C	41 ± 4	42 ± 4
		Rx	2 ± 3	6 ± 4
pH		C	7.39 ± 0.03	7.36 ± 0.04
		Rx	0.002 ± 0.005	0.01 ± 0.03
pCO_2		C	35 ± 3	35 ± 2
		Rx	1 ± 5	-2 ± 3

*Treatment values expressed as the mean change relative to control values. $\bar{X}$ ± SD; S = systolic; D = diastolic; C = control; Rx = treatment period.

The remaining factors of weight and fluid administration are summarized by group and response to treatment in Table 5. No significant differences were evident between treatment groups or between the different responses to treatment. The wide range of fluid replacement required to maintain systemic blood pressure and normalize the hematocrit during the experimental series, however, is reflected in the large standard deviations shown in this table.

DISCUSSION

The principal reason for the development of this model was to investigate aspects of treatment of spinal cord DCS (Leitch, 1984). Furthermore, the model was designed to simulate as closely as possible the effects of delay in treatment because the great majority of human spinal cord DCS is treated only after considerable delay, usually as the result of failure to diagnose the condition initially, followed by delay in transporting the patient to a treatment facility. It is well recognized that delay in instituting therapy may result in a therapeutic outcome that is less than optimal. For this reason, therapy was delayed in the model for 15 min to allow the lesion of spinal cord DCS to consolidate. Although the model cannot be compared directly to the human experience, there are parallels that suggest that it does indeed reflect the human experience. The very wide response to any type of therapy is seen in patients where the therapeutic response varies from excellent, with complete resolution of symptoms and signs, to poor, with varying degrees of sensory and motor deficits. A similar picture was seen in the model where the electrophysiological measure of spinal cord function also varied from an excellent return of amplitude of the SEP to those animals in which return was minimal. Because the majority of animals, regardless of treatment group, did not experience a return to predive surface control values, however, it could be argued that this animal model is more severe than

TABLE 3

CONTROL AND TREATMENT VALUES BY TREATMENT GROUP*

			Group A	Group B
Aortic Pressure (mm Hg)	(S)	C	150 ± 18	130 ± 13
		Rx	<1 ± 17	<1 ± 17 NS
	(D)	C	119 ± 15	100 ± 16
		Rx	-2 ± 14	<1 ± 17 NS
Right Ventricular Pressure (mm Hg)	(S)	C	18 ± 8	22 ± 6
		Rx	-3 ± 5	5 ± 8†
	(D)	C	2 ± 2	1 ± 1
		Rx	2 ± 2	6 ± 7 NS
CSF Pressure (mm Hg)	(S)	C	4 ± 3	6 ± 3
		Rx	14 ± 18	19 ± 18 NS
	(D)	C	4 ± 4	4 ± 3
		Rx	13 ± 16	18 ± 17 NS
Heart Rate		C	131 ± 29	127 ± 19
		Rx	-11 ± 22	-1 ± 10 NS
Rectal Temperature		C	38.19 ± 0.09	37.82 ± 0.49
		Rx	-0.12 ± 1.06	0.32 ± 0.79 NS
Hematocrit		C	43 ± 4	40 ± 4
		Rx	4 ± 5	4 ± 2 NS
pH		C	7.38 ± 0.03	7.30 ± 0.05
		Rx	0.03 ± 0.06	0.001 ± 0.03 NS
pCO_2		C	35 ± 2	34 ± 2
		Rx	-1 ± 3	-<1 ± 6 NS

*Treatment values expressed as the mean change relative to control values. $\bar{X}$ ± SD; S = systolic; D = diastolic; C = control period; Rx = treatment period.

† $p < 0.05$

interval, reflecting onset time and the severity of the insult, measured immediately before treatment.

Reanalysis of the results regarding treatment group after removal of the nonresponders uncovered a difference between the treatment groups. The initial response, measured by intercept, showed a trend in favor of Group B. Similarly, there was a significant difference in gradient in favor of Group A. As before, extrapolation of the linear regression line was performed to estimate the outcome at 120 min, and no significant difference in outcome was found with the nonresponders removed from the analysis.

II. Physiological Measurements.

Table 3 summarizes the measurements during the control period, together with the mean differences during the treatment period. No major physiological change occurred in either treatment group, except a moderate rise in CSF pressure. This change was of similar magnitude in both treatment groups. In general, the other changes that occurred were small and parallel in both treatment groups. The only exception to this observation occurred in the systolic pressure in the right ventricle. In Group A there was a mean fall of 3 mm Hg, whereas in Group B a mean rise of 5 mm Hg occurred. This was statistically significant, but as it occurred in isolation, it is difficult to interpret in physiological terms. It can be seen that each group also had similar control values. Regarding aortic pressure (both systolic and diastolic), however, Group B had lower pressures. In terms of separation into responders and nonresponders, both groups were similar during the control period. The differences during treatment show that systemic blood pressure was lower in the nonresponders and that the rise in CSF pressure was much greater in this group. There was also a tendency for the nonresponders to show a greater degree of hemoconcentration.

TABLE 2

ONSET, SEVERITY, AND COURSE OF TREATMENT WITH RESPECT TO RESPONSE*
(TREATMENT GROUPS A AND B COMBINED)

Treatment Group	Surface Interval (min)	SEP at Start Rx (%)	Intercept (%)	Gradient	Response at 120 min Rx (%)
Responders (n = 11)	27.0 ± 10.0	26.2 ± 21.0	77.17 ± 18.09	-0.0314 ± 0.117	73.48 ± 13.97
Nonresponders (n = 7)	19.0 ± 3.0	10.04 ± 13.37	24.26 ± 3.99	-0.042 ± 0.09	19.22 ± 13.17

* ($\overline{X}$ ± SD)

TABLE 1

ONSET, SEVERITY, AND RESPONSE WITH RESPECT TO TREATMENT*

I. All animals

Treatment Group	Surface Interval (min)	SEP at Start Rx (%)	Intercept (%)	Gradient (%/min)	Response at 120 min Rx (%)
A (n = 10)	23.5 ± 7.7	21.5 ± 24.4	57.15 ± 25.01	0.0043 ± 0.085	57.67 ± 28.7
B (n = 8)	24.5 ± 9.8	17.96 ± 13.4	55.9 ± 38.31	-0.0853† ± 0.0112	45.77 ± 32.8
II. Nonresponders excluded					
A (n = 7)	25.0 ± 8.8	30.49 ± 24.01	70.48 ± 12.1	0.0187 ± 0.0856	72.73 ± 16.81
B (n = 4)	30.5 ± 10.8	18.76 ± 14.66	88.88 ± 22.61	-0.1191† ± 0.121	74.81 ± 9.03

* ($\bar{X}$ ± SD)
† $p \leq .05$

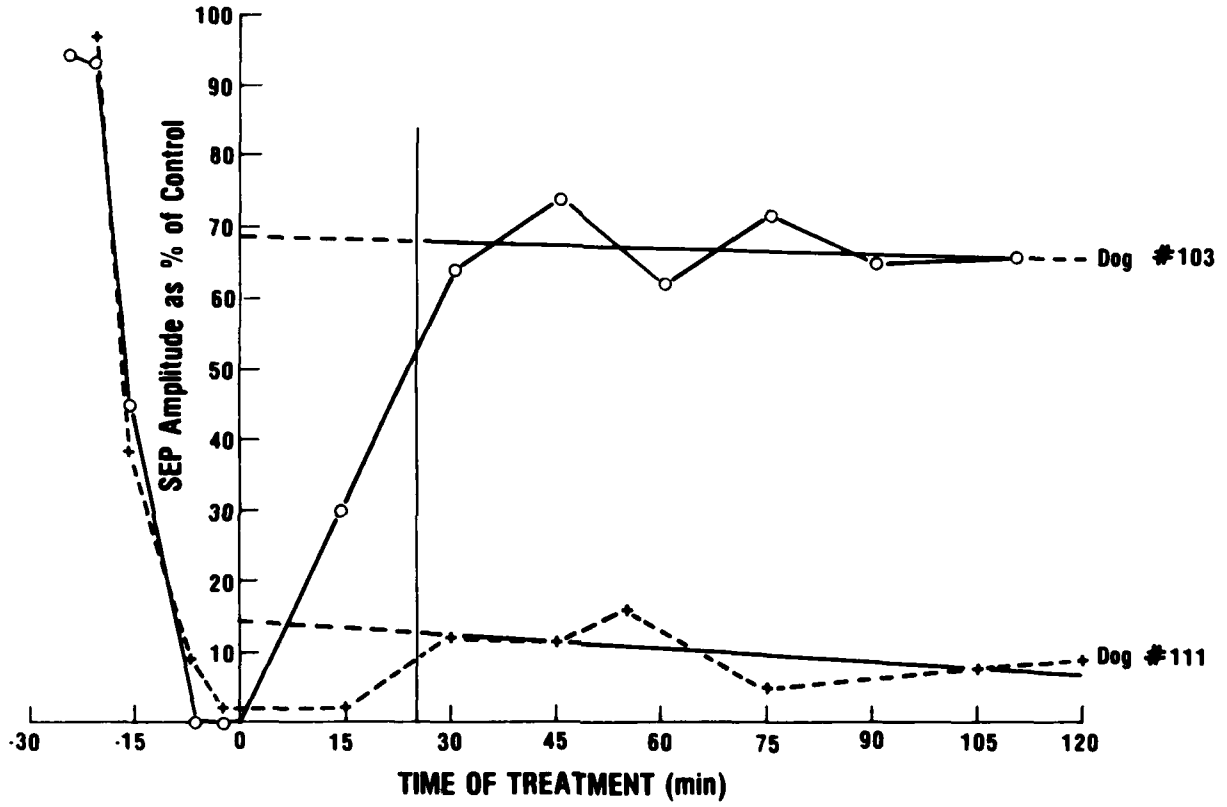

Fig. 1. Examples of recovery of SEP amplitude during treatment. Data from +25 to +120 were fitted to a straight line for each animal. Slope and intercept were incorporated in Tables 1 and 2.

final recording of SEP before treatment this ranged from a 27.3-100% loss compared to surface control values with mean values of 21.5 ± 24.4% and 17.96 ± 13.4% for Group A and B, respectively.

Initial inspection of the data with respect to the effects of treatment showed an early, rapid response, regardless of treatment group. This effect was generally complete between 15 and 30 min of treatment, after which no further obvious improvement occurred. The magnitude of the response to treatment varied considerably, again regardless of treatment group, ranging from a minimal response to a return to more than 90% of surface control values. Consequently, we decided to fit linear regression lines to each animal's response data from 25 min of treatment onward, and to use the intercept as a measure of response and the gradient as a measure of progress during the treatment (Fig. 1). The results of this analysis and the onset data are summarized in Table 1, which shows that there is no difference (Student's t test) between the surface interval before treatment, the severity of DCS, and the response to treatment. Despite a slight difference in gradient ($p \leq .05$) in favor of Group A, however, there is no difference in the calculated outcome at 120 min (2 hr) of treatment, although the trend towards a less successful outcome for Group B is detectable from the gradient.

In addition to the wide response to treatment, it was also evident from the inspection of the data that there was a separation of response into two groups: either a "good" result or a "poor" result, independent of treatment group (Fig. 1). A similar analysis was performed from data corresponding to this aspect of the response to treatment, designating an actual return to 50% of surface values as an arbitrary separation into "responders" and "nonresponders." The clear separation of the two categories is evident from Table 2. It is also clear that there is a significant difference in surface

theoretical, lies in subjecting a patient, already suffering from a decompression insult, to additional exposure to inert gas, and therefore, a decompression obligation at a time when mechanisms for the elimination of inert gas may be compromised. Secondly, it introduces yet another choice of therapeutic table into an already confusing array of possible choices. Thirdly, it involves enormous logistical problems in supplying a nonstandard gas mixture throughout the US Navy and possibly to NATO in the long term.

6. Because no therapeutic advantage to the use of this treatment regime has been determined, the advantages of its increased safety will have to be balanced against the disadvantage of additional inert gas loading, the logistics of supply, and the potential for introducing more confusion into the treatment armamentarium.

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